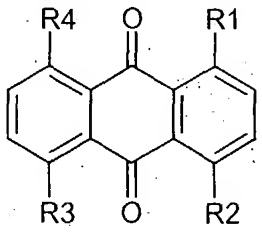
## ABSTRACT

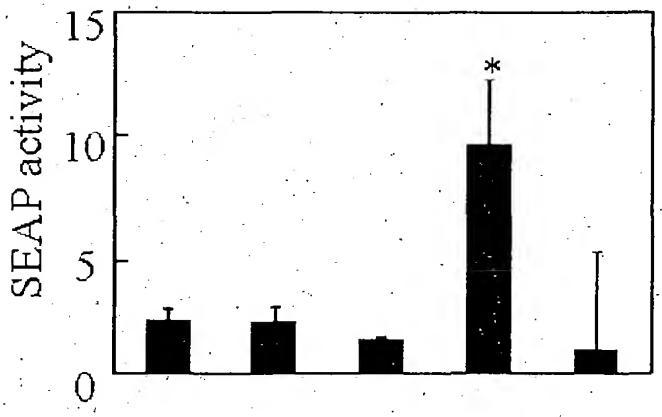
This invention relates to novel anthraquinone compounds useful in the treatment of allergic, inflammatory conditions, antioxidant, tumor condition, stem cell application, tissue engineering, applied in treating age-associate tissue degeneration, reverse organ failure in chronic high-turnover disease and therapeutic compositions containing such compounds. The compounds of the present invention are 1,4-, 1,5- and 1,8-difunctionalized anthraquinones or analogs thereof. According to the practice of the invention, there are provided bis-symmetrical substituted anthraquinone compounds according to formula I:




FORMULA I

wherein R1, R2, R3 and R4 present a straight, aminoalkylamino side chains or branched chain alkyl group having 1 to 6 carbons which may be substituted with one or more groups of R5, or R1, R2, R3 and R4 present phenyl or benzyl which may be substituted with one or two groups of R6; wherein R5 is selected from the group consisting of halogen, $-RNH_2$, $-RNH_2R$, $-ROH$, $-NO_2$, $-OCH_3$, $-OCH_2CH_3$, and $-OCH_2CH_2CH_3$; and wherein R6 is selected from the group consisting of a straight or branched chain alkyl group having 1 to 4 carbons, halogen, $-RNH_2$, $-RNH_2R$, $-ROH$, $-NO_2$, $-OCH_3$, $-OCH_2CH_3$, $-OCH_2CH_2CH_3$, $-CH_2Br$, $-CH_2Cl$, $-CH_2OH$, $-C(CH_3)_3$, $-(CH_2)_2OH$, $-(CH_2)_3OH$, $-(CH_2)_4OH$, $-CH_2NH_2$, $-(CH_2)_2NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_5NH_2$, $-CH_2N(CH_3)_2$, $-(CH_2)_2N(CH_3)_2$, $-(CH_2)_2NH(CH_2)_2OH$, $-(CH_2)_3NH(CH_2)_2OH$, $-(CH_2)_2NHCH_2OH$, $-(CH_2)_3NHCH_2OH$, $-CH_2CH(CH_3)_2$, $-CHCl_2$, $-CH(CH_3)Cl$, $-(CH_2)_2Cl$, $-(CH_2)_3Cl$, $-(CH_2)_3Br$, $-(CH_2)_4Br$, and $-(CH_2)_4Cl$.

Chart 1. Activation of *hTERT* promoter-driven SEAP expression by c-Myc. About 1 x $10^7$ hTERT-BJ1 cells were transfected with 13.5 μg each of plasmid pSEAP or pPhTERT-SEAP and of plasmid pMT2T or pMT2T-cMyc by electroporation. After 24 h, viable cells were harvested, and reinoculated at a density of 3 x $10^5$/mL, and the SEAP activity after 24 h at 37 □. The transfection efficiency of each experiment was determined by cotransfection with 1.5 μg of plasmid pCMVβ. The values were determined from three experiments. $P < 0.05$ is presented by an asterisk.




| | | | | | |
|---|---|---|---|---|---|
| pSEAP | + | - | + | - | - |
| $pP_{hTERT}$-SEAP | - | + | - | + | - |
| pMT2T | + | + | - | - | - |
| pMT2T-cMyc | - | - | + | + | - |

Chart 2. Stable cell lines harboring $P_{hTERT}$-SEAP did not affect the growth rate of their parental cell lines. H1299, hTERT-BJ1, and stable cell lines harboring $P_{hTERT}$-SEAP were grown at 37 □ in the presence of 5% $CO_2$. The cell growth was monitored for a period of 96 h using MTT assay. The values are determined from four experiments.

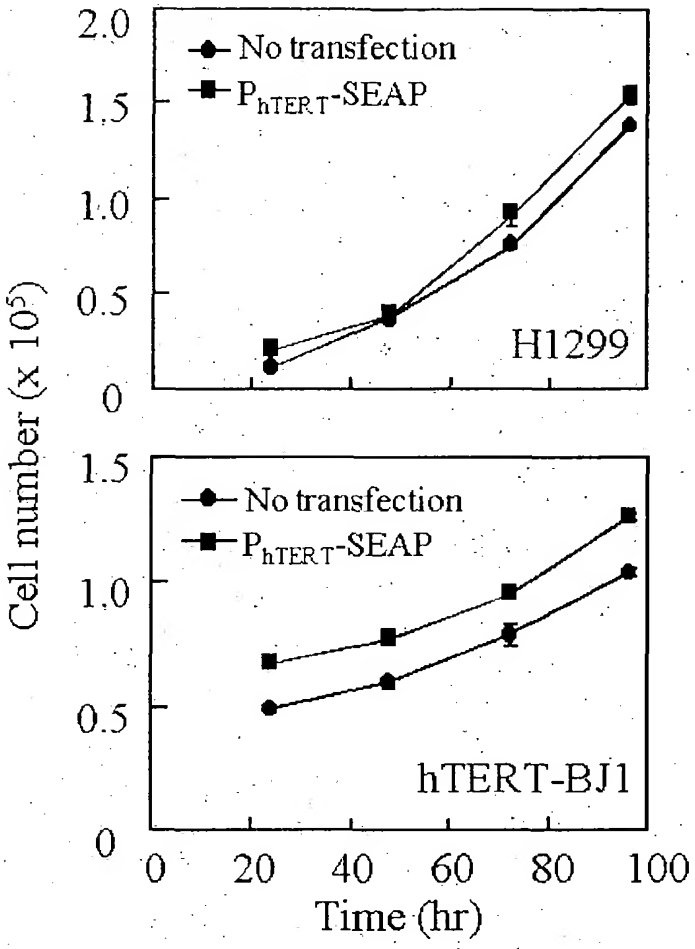


Chart 3. Expression of $P_{hTERT}$-SEAP in H1299 cells and lack of $P_{hTERT}$-SEAP expression in hTERT-BJ1 cells. H1299, hTERT-BJ1, and stable cell lines harboring $P_{hTERT}$-SEAP from these two cells were analyzed for SEAP activity. The values are determined from three experiments.

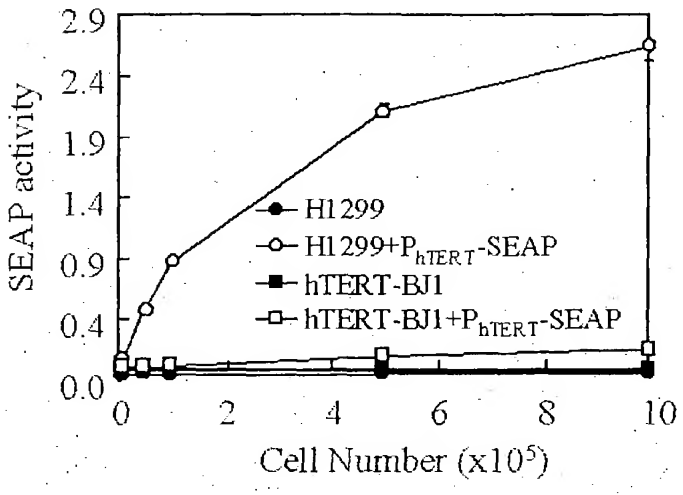


Chart 4. Specific activation of $P_{hTERT}$-SEAP by analogues of anthraquinone. About 2 x $10^3$ cells of hTERT-BJ1 harboring $P_{hTERT}$-SEAP or $P_{CMV}$-SEAP were seeded in 96-well plates and incubated at 37 □ for 24 h. Cells were then washed with PBS, recultured in fresh media, and incubated with varying amounts of IIIi, IIIa, or IIId for another 48 h. The culture media were collected and subjected to SEAP activity analysis. The level of cell growth was also determined using MTT assay. The values are obtained from six experiments using the values without drug treatment as 100%.